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SELF-ORGANIZED CRITICALITY AND STOCHASTIC RESONANCE IN THE HUMAN BRAIN

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Abstract

The human brain spontaneously generates neuronal network oscillations at around 10 and 20 Hz with a large variability in amplitude, duration, and recurrence. Despite more than 70 years of research, the complex dynamics and functional significance of these oscillations have remained poorly understood.

This Thesis concerns the dynamic character and functional significance of noninvasively recorded 10- and 20-Hz oscillations in the human brain. The hypotheses, experimental paradigms, data analyses, and interpretations of the results are inspired by recent insights from physics—most notable the theory of self-organized criticality and the phenomenon of stochastic resonance whose applicability to large-scale neuronal networks is explained.

We show that amplitude fluctuations of 10- and 20-Hz oscillations during wakeful rest are correlated over thousands of oscillation cycles and that the decay of temporal correlations exhibits power-law scaling behavior. However, when these ongoing oscillations are perturbed with sensory stimuli, the amplitude attenuates quickly, reliably, and transiently, and the long-range temporal dynamics is affected as evidenced by changes in scaling exponents compared to rest. In addition to the rich temporal dynamics in local areas of the cortex, ongoing oscillations tend to synchronize their phases and exhibit correlated amplitude fluctuations across the two hemispheres, as shown for oscillations in homologous areas of the sensorimotor cortices. Finally, it is revealed that intermediate amplitude levels of ongoing oscillations provide the optimal oscillatory state of the sensorimotor cortex for reliable and quick conscious detection of weak somatosensory stimuli.

We propose that the long-range temporal correlations, the power-law scaling behavior, the high susceptibility to stimulus perturbations, and the large amplitude variability of ongoing oscillations may find a unifying explanation within the theory of self-organized criticality. This theory offers a general mechanism for the ubiquitous emergence of complex dynamics with power-law decay of spatiotemporal correlations in non-linear self-organizing stochastic systems consisting of many units. The optimal ability to detect consciously and respond behaviorally to weak somatosensory stimuli at intermediate levels of ongoing sensorimotor oscillations is attributed to stochastic resonance—the intuitively paradoxical phenomenon that the signal-to-noise ratio of detecting or transmitting a signal in a non-linear system can be enhanced by noise.

Based on the above results, we conjecture that a mechanism of intrinsic stochastic resonance between self-organized critical and stimulus-induced activities may be a general organizing principle of great importance for central nervous system function and account for some of the variability in the way we perceive and react to the outside world.

Keywords

Neuroscience; complexity physics; neuronal population dynamics; avalanche dynamics; spontaneous or ongoing oscillations; self-organization; variability; criticality; brain states; stochastic resonance; correlations; scaling behavior.

List of publications

This Thesis is based on the following publications:

P1
Linkenkaer-Hansen K, Nikouline VV, Palva JM, Ilmoniemi RJ. Long-range temporal correlations and scaling behavior in human brain oscillations. *The Journal of Neuroscience*, 21:1370–1377, 2001.

P2
Nikouline VV, Wikström H, Linkenkaer-Hansen K, Kesäniemi M, Ilmoniemi RJ, Huttunen J. Somatosensory evoked magnetic fields: relation to pre-stimulus mu rhythm. *Clinical Neurophysiology* 111:1227–1233, 2000.

P3
Nikouline VV, Linkenkaer-Hansen K, Wikström H, Kesäniemi M, Antonova EV, Ilmoniemi RJ, Huttunen J. Dynamics of mu-rhythm suppression caused by median nerve stimulation: a magnetoencephalographic study in human subjects. *Neuroscience Letters* 294:163–166, 2000.

P4
Nikouline VV, Linkenkaer-Hansen K, Huttunen J, Ilmoniemi RJ. Interhemispheric phase synchrony and amplitude correlation of spontaneous beta oscillations in human subjects: a magnetoencephalographic study. *NeuroReport* 12:2487–2491, 2001.

P5
Linkenkaer-Hansen K, Nikulin VV, Palva JM, Kaila K, Ilmoniemi RJ. Stimulus-induced change in long-range temporal correlations and scaling behavior of sensorimotor oscillations. TKK–F–A815 (2002). ISSN: 1456–3320. ISBN: 951–22–6176–6.

P6
Linkenkaer-Hansen K, Nikulin VV, Palva S, Ilmoniemi RJ, Palva JM. Intrinsic stochastic resonance of sensorimotor processing mediated by ongoing neuronal oscillations. TKK–F–A816 (2002). ISSN: 1456–3320. ISBN: 951–22–6177–4.

Contribution of the author

I conceived the original idea and experimental paradigm, conducted the experiments, wrote the analysis software, analyzed the data, and was the principal and corresponding author of publications P1, P5, and P6. In publications P2–P4, I participated actively in discussing the analyses, results, and in writing the manuscript.

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Helsinki, October 2002

Klaus Linkenkaer-Hansen

Contents

1 Introduction

This Thesis concerns the nature of oscillatory activity in the human brain, in particular at 10 and 20 Hz. These oscillations are generated spontaneously in several areas of the cerebral cortex as neuronal networks transiently form assemblies of synchronously firing cells. Sensory input can modulate or induce neuronal activity at around 10 and 20 Hz, but a large variability in amplitude, duration, and recurrence of these oscillations is observed even in the absence of such perturbations. This variability has intrigued researchers for more than 70 years [19,83,92], yet its mechanistic origin and functional significance have remained poorly understood.

To understand the source of variability in spontaneously generated or stimulus-induced neuronal oscillations, it seems intuitively natural to investigate the detailed biophysical mechanisms underlying the generation of this activity. Nevertheless, there may be an alternative approach. Recent years of research on self-organization and complexity has lead to novel methods and frameworks for analyzing and interpreting variability *per se*, which are now changing the way complex fluctuations are perceived in many areas of science [12, 27, 56, 145]. While previously considered a nuisance or "noise", *variability is increasingly being acknowledged as a potentially valuable source of information about the developmental history and spatiotemporal organization of non-linear dynamical systems.*

The central premise of the present work is that theories of self-organization, aiming to explain the often statistically stereotyped variability of structures and dynamics in systems consisting of many non-linearly interacting units, may also apply to the dynamics of 10- and 20-Hz oscillations in the brain. The most fundamental prediction of these theories is a "critical" type of dynamics of these network oscillations, which should be reflected in intermittent amplitude fluctuations with a slow power-law decay of the temporal correlations. We further hypothesized that the interaction between ongoing and stimulus-induced activities may give rise to stochastic-resonance effects in perception and behavior. Finally, it is conjectured that network oscillations in a critical state may provide a beneficial susceptibility for the brain to detect weak inputs and to reorganize swiftly from one state to another during processing demands.

To summarize in neuroscientific terms, the aim of this Thesis is to characterize the state of the brain during wakeful rest, as indexed by 10- and 20-Hz oscillations, and how this state is affected by and affects the processing of incoming information from our sensory environment.

1.1 Outline of the Thesis

Throughout this Thesis, I treat the relevance and limitations of certain theoretical frameworks of non-linear dynamical systems, self-organization, and complexity to the field of neuroscience and review the main results of publications P1–P6.

Section 2 outlines one of the greatest challenges for a "theory of the brain" and its relationship to complexity science. Sections 3.1–3.3 introduce a number of neuronal phenomena that are important for understanding the origin and character of complexity in the central nervous system. Several terms and concepts are defined in order to put the neuroscientist and the physicist on an equal footing. The scientific fields of self-organization and complexity are defined in Section 3.4 with the aim of establishing the neuronal equivalence of the prerequisites for non-linear systems to self-organize to a critical state. Different classes of stochastic resonance are treated in Section 3.5. The main aims and the essential methods of the studies are listed in Sections 4 and 5, respectively. The main results of publications P1–P6 are summarized in Section 6. A general discussion with outlook and perspectives is found in Section 7 followed by the main conclusions in Section 8.

2 Theories of complexity and the brain

To appreciate the scope and potential of complexity theories in neuroscience, it is instructive to reflect on the traditional method of science and what I consider one of the greatest challenges in "brain theory".

2.1 Reductionism and the fragmentation of science

Science aims to discover and characterize natural phenomena in order to improve our understanding of causes and effects in nature. To this end, the reductionistic approach has proven successful in many respects; however, it has also caused science to divert into innumerable branches in an attempt to cope with the surge in information about phenomena on different temporal and spatial scales. Moreover, structural and dynamical properties are often studied separately even when they are intimately related, thereby dismissing causal relations that span several orders of magnitude in time and/or space and compromising the intellectual integrity of science [70].

2.2 A major challenge for "brain theory"

The brain is complex at all levels of organization from the morphology and activity patterns of the individual neurons to the circuitry and population activity of large-scale networks involving millions of neurons. The large-scale activity that emerges from the cooperative action of many neurons may in turn exert a determining influence on the morphological development and activity of individual neurons. These mechanisms give rise to a type of "reciprocal causality" that further complicates our choice of scale of investigation when attempting to trace the causes and effects as the brain develops and refines its spatiotemporal organization in response to the past and preparation for the future.

The diversity of tasks performed by the brain naturally gives rise to some flexibility in the definition of what to include in a "theory of the brain". In fact, there has been widespread skepticism among neurobiologists whether the concept of theory in neuroscience at all makes sense [126]. Indeed, several models aim to account for various neuronal phenomena, but only few theories are able to identify general organizing principles of the brain. I would mention the "temporal correlation hypothesis" as an exception [75, 119], although several theoretical issues still need to be clarified and supported by empirical evidence before it can be established as a general coding scheme in neuronal systems.

Without theories, however, it is no surprise that neuroscience is characterized by little integrity between its many disciplines, even though the need for integrity is maybe more pronounced in neuroscience than in any other science. Simple questions like why alcohol makes us feel drunk require an integral description of neuronal function at the transmitter and receptor level to the large-scale neuronal activity that presumably is needed for cognition to emerge.

Thus, a theory of the brain is challenged by the need for detailed characterization of neuronal systems on a wide range of spatial and temporal scales while retaining the global picture of how the structures and dynamics at these different levels emerge and work together in the normal functioning brain.

2.3 Power laws and natural integrity

Theories of self-organization and complexity provide a complementary approach to the traditional specialization into narrowly defined fields of science. Instead of choosing a narrowly defined scale of interest, complexity studies search for similarities in statistics of the spatiotemporal organization of complex systems across several orders of magnitude. Furthermore,

general mechanisms for generating this complexity are being formulated and analogies between different systems are being established. Complexity science therefore holds the promise of providing insight into the problem of how systems with large variability in structures and dynamics on many scales arrive at this organization. This field of science has been motivated by the fact that several animate and inanimate systems exhibit structural and dynamical complexity even though the laws of physics that govern the interactions between the elements of these systems are usually simple. Moreover, the complexity often obeys power-law statistics over a wide range of temporal and/or spatial scales.

Briefly stated, the significance of power-law functions in our context is related to the complex variability of shapes that they can characterize and their slow decay compared with the exponential functions that are also prominent in statistics. Power laws are fundamental signatures of complexity and play a crucial role in this Thesis. Therefore, this mathematical relation and its significance in statistics will be described.

Mandelbrot pioneered the analysis of complex shapes and time-series signals, which he termed *fractals* [27] (p. 45). He discovered that many processes often look roughly the same when viewed at different levels of magnification, i.e., the same patterns are repeated on many different scales (buy a cauliflower to see what this means!). This feature of fractals is termed *self-similarity* or *scale-invariance* and it is captured by the power law with the following mathematical form:

$$P(f) = f^{-\beta} \tag{1}$$

Equation 1 is the example of $1/f$-noise and states that the power spectral density, P, of a signal is proportional to the frequency, f, raised to the power $-\beta$. Thus, the power-law exponent β expresses how P and f scale with respect to each other and is therefore termed the *scaling exponent*. Many dynamical systems are characterized by a scaling exponent close to 1 in the power spectrum (therefore the term $1/f$-noise). Using this example, one can appreciate the scale-invariance of the power law: determine the power spectral density at a low frequency (a long time scale), then double the frequency (i.e., cut the time scale in half) and P decreases a factor of two. Cut the time scale in half again and P decreases yet a factor of two, etc. In other words, by decreasing the time scale one may zoom in on finer and finer details of the time series to discover ever-smaller fluctuations that keep having the same qualitative relationship with those on the preceding longer time scale. This is true for any scale in the range where the power law is valid and only power laws have this unique feature of scale-invariance [27] (p. 41).

In order to understand the significance of scale-invariance, let us first contrast it with another typical statistic: the presence of preferred or *characteristic* scales in the underlying system as reflected in peaks or bends on the curves that characterize its spatial or temporal organization. The probability of deviations from the mean of a characteristic scale is usually

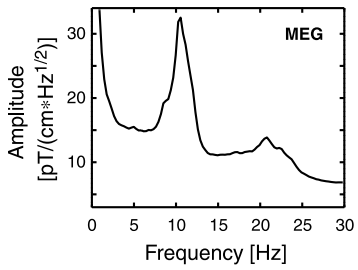

Figure 1: The grand average ($n = 10$) amplitude spectrum of raw broadband MEG signals from channels over the right sensorimotor region in a condition of eyes closed. Note the clear peaks at around 10 and 20 Hz indicating characteristic time scales of the underlying neuronal interactions of about 100 and 50 ms, respectively.

characterized by the normal distribution or some other function with exponential tails, i.e., it becomes "exponentially unlikely" to encounter large deviations and prohibitively unlikely that mechanisms with preferred scales yield values that exceed the mean by several orders of magnitude. The power spectrum of spontaneous human MEG signals is a good example of a relation that is *not* scale-invariant (Fig. 1). Depending on the experimental condition and anatomical region of recording the electric activity, peaks are found, e.g., at around 6, 10, 20, and/or 40 Hz, which may reflect distinct neuronal populations or mechanisms of generating these oscillatory activities. Conversely for the scale-invariant case, it is commonly—and tacitly—assumed that a change in mechanism would cause a deviation from the power-law curve or affect the scaling exponent [18, 104]. In other words, *one may interpret the absence of distinct scales as an indication that the structures and/or dynamics are governed by a single mechanism on all the scales where the power law applies.*

A "single mechanism" is defined as a set of rules that can be expressed mathematically (i.e., with equations). It should be emphasized that the physico-chemical processes involved may be complicated. This in turn implies that the fairly rare events in the tails of power-law distributions should not be viewed as "noisy outliers", but rather as the natural consequence of some underlying mechanism. This is one of the reasons why it is significant to reveal power laws in complex systems, i.e., *the scale-invariance indicates that "rare events" are actually not rare at all from a statistical point of view.*

Notable examples of scale-invariance that have attracted widespread attention (and some controversy) include the dynamical organization of financial markets and earthquakes. The probability of a price change on a stock market or an earthquake to have a certain magnitude is governed by a power law spanning eight orders of magnitude (a factor of 10^8) [13, 122]. In view of the above reasoning, these statistical laws suggest that financial crashes or the devastating earthquakes have no different dynamics, underlying cause or mechanism than those that cause small changes to stock prices every minute or barely detectable movements of the earth's crust. This perspective has greatly challenged conventional models of financial systems and earthquakes in which large events are considered "rare" and thought to require special explanations [12, 27].

Another important implication of the tendency of complex systems to develop scale-invariance is that the recurrence of similar patterns on different scales reflects a sort of natural integrity, i.e., structures and/or dynamics unavoidably become correlated on all scales. But what is the source of this highly organized non-randomness? The physics underlying this phenomenon is treated in detail in Section 3.4.1, but qualitatively speaking it has to do with the accumulation of internal constraints to the dynamics that many self-organizing systems unavoidably produce as a consequence of the formation of spatially correlated structures, i.e., simple features of geometry that control how influences propagate [27]. This insight has been gained primarily through the use of so-called *agent-based modeling*, a computer-simulation technique that is described in the following Section (2.4).

In summary, the widespread occurrence of power-law statistics in nature is surprising because such statistical similarities indicate that the spatiotemporal organization does not change when moving to smaller or larger scales of observation by orders of magnitude, which counterintuitively suggests that the same mechanisms operate on widely different scales.

2.4 Agent-based modeling: large-scale dynamics "bottom-up"

The laws that describe the behavior of a complex system are qualitatively different from those that govern its units, a phenomenon often denoted *emergence* [145]. Agent-based modeling is a computer technique that has contributed significantly to our current understanding of emergence in high-dimensional systems by simulating the evolution of systems consisting of many agents or units on the basis of a set of rules that typically express how neighboring units interact [22]. Cellular automata is another term for the agent-based modeling approach

and a large resource on its far-reaching potential for explaining the emergence of complex structures has recently been published by Stephen Wolfram [148].

Agent-based modeling can be used for the study of growing spatial structures in networks, how these structures influence the dynamics of distributed systems, or even the creation of various spatiotemporal phenomena, which are impossible to anticipate on the basis of the rules that govern the individual agents. In other words, numerical simulations are essential for the study of the emergence of structures and dynamics in complex systems because of their dependence on their own history. A well-known example of this is John Conways "Game of Life", where initially randomly organized units assemble without external guidance into groups of varying sizes and with distinct behaviors after a period of self-organization [10].

The untraditional approach that has gained popularity and very much defined the science of complexity is to search for scale-invariance and to use the power-law scaling exponents as a compact way to characterize complex structures or dynamics, and subsequently try to simulate the large-scale dynamics using agent-based modeling of which the successful model will exhibit the same scaling behavior [66, 67]. Because of the generality of the rules that lead to spatiotemporal complexity, different systems may be characterized by identical scaling exponents, which is the basis for grouping a wide range of phenomena into universality classes [16] (p. 258–297) and for establishing analogies between completely different systems. This has been done, e.g., between energy transfer in fully developed turbulence and information transfer in foreign currency exchange markets [53]. Recent progress along these lines includes linking several independently derived scaling exponents into a *scaling law*, which provides more strict criteria for the comparison of different systems and/or for holding models against empirical data [13, 100, 116].

In retrospect, the success of agent-based modeling for generating complex spatiotemporal behavior is not so surprising given the ubiquity of power-law scaling behavior and the significance of power laws. As argued in Section 2.3, one may regard all the structures and/or dynamics that fall in the range of a power law to have the same mechanistic origin—or "set of rules" [22]—but this, in turn, is how agent-based modeling is defined. The challenge is to deduce the rules and express them mathematically in order to incorporate them in simple algorithms. While this may seem easier said than done, two aspects facilitate the approach. First of all, it turns out that the mechanism responsible for the generation of the large-scale spatio-temporal organization in many nonlinear non-equilibrium systems may be given a very general formulation. It does not rely much on the complex microscopic details, but simple underlying features of geometry that control how influences propagate [27] (p. 92). The detailed prerequisites for this situation are given in Section 3.4.1. Second of all, it is conceivable that nature needs to employ complicated mechanisms in order to implement a certain rule that can be expressed mathematically in fairly compact and simple ways. However, I believe that it is the rule more than the mechanism for achieving the rule that matters for brain function.

Methods that are similar to those of agent-based modeling are also employed in computational neuroscience. The tradition has, however, more been that of a top-down approach [71], i.e., to investigate the phase space of a number of coupled differential equations and identify parameter settings that can reproduce a certain qualitatively or quantitatively defined behavior, rather than letting a high-dimensional model system "grow its own dynamics" as it happens in nature and in agent-based modeling.

In summary, one may gain insight into how the structures and dynamics at different levels of neuronal organization emerge and work together in the normal functioning brain (cf. Section 2.2) by searching for scale-invariant structures and dynamics in the brain, and subsequently employ the agent-based modeling approach to arrive at a mathematical formulation of the rules that govern the given scale-free phenomenon. From this point of view, traditional neuroscience investigates nature's physico-chemical implementation of *rules* rather than revealing the basic principles of operation as defined by these rules.

3 Overview of the literature

In the following Sections (3.1–3.5), a number of characteristics of neurons and neuronal networks are introduced and the correspondence between specialized terms of neuroscience and concepts in complexity sciences established.

3.1 Brain ontogeny and self-organization in neuronal systems

The macro-structural organization of the brain, such as the division of the cortex into hemispheres and the location of primary sensory areas in the cortex as well as subcortical structures, is relatively constant and mainly determined by the genetic code [70, 105]. The information contained in the human genome is, however, vastly insufficient to code for the microstructural wiring of the cortex involving the establishment of around 10^{14} synaptic connections between 10^{11} neurons [33]. Besides, the function of the brain is to a large extent to help us learn from experiences and adapt to and survive in an ever-changing environment, which cannot be encoded in the brain from birth [68].

Instead of following some master plan, the brain constructs itself in a complex interplay between internal constraints defined by the genetic makeup and a number of activity-dependent physico-chemical processes. While it has long been acknowledged that exogenous activity, i.e., neuronal activity driven by environmental influences through our senses, is crucial for the normal development of neuronal circuits [68, 105] (p. 1115–1130), recent years of research have also stressed the importance of *endogenously* generated activity as a strong determining factor in shaping the morphology of individual neurons and the topology of large-scale neuronal networks from early stages of development and throughout life [105]. The closely related terms "endogenous", "intrinsic", and "spontaneous" imply that the activity is generated from within the system, which may be viewed as synonymous to the term "self-organized", which is used in sciences of self-organization and complexity to denote dynamical changes that result from the interactions among components without explicit involvement from outside the system. Here "explicit" is added because some source of energy or driving force is needed to keep the usually dissipative systems going, as is also the case for neuronal systems.

Isolated neurons are generally thought to be able to fire an action potential spontaneously in a probabilistic manner that is random in the sense of being independent of previous activity, and often they are assumed to do so even when being part of a network [135]. There is, however, little justification for this "randomness assumption", since even down to the molecular scale of single Na^+ channels, activity-dependent structural constraints translate into a memory that affects the future neuronal excitability on time scales from milliseconds to minutes [135]. Moreover, electrical activity causes the release of neurotrophic factors that regulate the morphological development of neurons such as axonal and dendritic arborization [143], and the establishment of synaptic connections with neighboring neurons is also activity-dependent. Altogether, the cellular-level structural development causes electrical activity to propagate and reverberate in increasingly larger and more complex and integrated networks, which in turn exert an influence on the structure and function of individual neurons [143]. This type of interplay across many scales is often referred to as circular or reciprocal causality [134].

Tracing the causal links between the emerging forms on the one hand and neuronal network activity on the other hand is complicated both by the astronomical number of neurons involved and the slow and long process for many neuronal structures to emerge. Nevertheless, the path of a neuronal signal through the network is dependent on past activity on many temporal and spatial scales and in this sense the endogenous activity cannot be considered random. That these signals often appear random to us merely reflect our lack of knowledge or immature recording and signal processing technologies.

As mentioned briefly in Section 2.4, the reciprocal relationship between structural changes and temporal dynamics is a hallmark of complex self-organizing systems. Although the correspondence between past and present activity is intuitively clear, most self-organizing systems—including the brain—are also subjected to stochastic driving forces, which makes it highly non-trivial to reveal the non-randomness hidden in the complex response patterns of these systems [1,62,109]. The best one can do with empirical data at present is to analyze for temporal or spatiotemporal correlations, hoping to detect correlations that deviate from that of a random process and reveal its underlying mechanism, e.g., the tendency of a signal to follow the same path as previously possibly because of underlying structural constraints [138].

The connectivity of the internet was recently discovered to have self-organized into a scale-free network, and based on the potentially valid analogy with self-organized topologies in neuronal networks, it was speculated that the intricate complexity of the brain gives rise to a beneficial redundancy that renders neuronal networks largely immune to "internal failures" (e.g., broken functional connections) [2, 17, 139]. It remains to be shown whether the brain at large and/or in local anatomical regions *is* scale-free, and to what extent this statistical feature is crucial for the brain's impressive robustness of performance. Computational approaches are invaluable for the exploration of these issues.

In summary, one may view the brain as a self-organizing non-linear system with a rich variety of emergent structures and dynamics that reflects its developmental history. Insight into the character of self-organization processes and the mechanisms that shape their dynamics may therefore help us understand certain aspects of brain ontogeny.

3.2 Oscillations and resonance in neuronal networks

Neuronal network oscillations are prominent emergent large-scale phenomena generating bursts of neuronal firing at frequencies mainly between 1 and 200 Hz [38]. Their functional significance depends, e.g., on the frequency content, anatomical location, and/or mechanisms of generation. The growing list of neuronal functions that seem to involve oscillatory activity includes:

1. Specifying connectivity in developing neuronal circuits [79, 102].
2. "Binding" or coordination of distributed processing [29, 118, 119].
3. Regulating sleep-wakefulness [79].
4. Memory consolidation [115, 125].
5. Short- and long-term memory [29, 125, 133].
6. Timing in motor coordination [79].
7. Perception [112, 127].
8. Reference frame or context for incoming information [47, 79].
9. Attention [40, 44, 48, 149].

It is beyond the scope of this discussion to comment on this diversity of functions in detail, but some general comments are in place. Synchronously active neurons enhance their saliency because of temporal summation of synaptic potentials in the target cells [118,119]. Neuronal oscillations may therefore serve, in most of the above processes, to associate or segregate distributed neurons into coherent assemblies for joint processing [29]. This function has usually been assigned to the high-frequency gamma oscillations (30–100 Hz), but oscillations at lower frequencies may serve a similar function [29].

So-called "pacemaker cells" have intrinsic ionic properties that enable them to fire spontaneously with regular intervals during certain experimental conditions [58,79,124], but most *in vivo* oscillations attain their natural characteristics only when the complex synaptic interactions between different types of neurons and anatomical structures are intact [124,125].

Given the nonlinear character of neurons and the interconnectedness of neuronal networks, it seems unavoidable that resonance effects would appear. It therefore cannot be ruled out that certain oscillations are epiphenomena serving no function; it is at least known that they can become pathological, e.g., as in epileptic seizures [76] and Parkinsonian tremors [131]. On the other hand, the abundance of correlations that have been identified between oscillation strength and/or synchrony and neuronal function renders it likely that even more of such functional correlations are to be discovered.

3.3 Network oscillations at 10 and 20 Hz

Network oscillations at around 10 and 20 Hz are particularly pronounced during wakeful rest when they emerge spontaneously in primary sensory areas and the motor cortex [41, 92]. Depending on the experimental condition, however, 10- and 20-Hz oscillations can be suppressed or increased transiently by various stimuli [50, 92, 95, 106, 108] or tasks [52, 65]. To leave open to what extent they are spontaneously or endogenously generated vs. modulated by externally imposed processing demands, such oscillations are termed "ongoing oscillations" in this Thesis. Based on the location of their cortical generators and reactivity to sensory input, 10-Hz oscillations have traditionally been denoted alpha (occipital and parietal) [92], mu (sensorimotor) [92], and more recently tau (auditory) rhythms [59], but here they are referred to by their center frequency and when appropriate also the macroanatomical location.

Evidence suggests that the generation of 10-Hz oscillations depends on interactions between thalamocortical and cortico-cortical systems [81, 124], but the cellular mechanisms and neuronal circuits underlying these oscillations remain poorly characterized. The cortico-cortical mechanisms seem likely to give rise to the phenomenon of a wave that travels or propagates in the tangential plane of the cortex [80] and may play an important role for the large-scale organization of 10-Hz oscillations as discussed further in Section 3.4.1.

The posterior 10-Hz oscillations are absent in babies less than 4 months of age, after which they emerge as a slow 4-Hz oscillation, increasing to 6, 8, and 10 Hz at the age of 1, 3, and 10 years, respectively [92]. The ontogeny of alpha rhythms is therefore a good example of a neuronal process that exhibits changes in dynamics on very long time scales.

Despite the long tradition of studying the alpha rhythm, there is no consensus about its functional significance. The tendency of 10-Hz oscillations to emerge during rest and to be suppressed when the given brain region is activated have earned them the name "idling rhythms" [59]. Although possibly idling for no good reason, it has also been speculated that this activity keeps neuronal networks in a state of readiness to respond quickly, e.g., by setting the mean level of the membrane potential within extensive populations of neurons and thereby affecting their input-output transfer function [82]—a possibility that is elaborated further in Section 3.5.

3.3.1 Low-dimensional chaos in 10-Hz oscillations?

The conspicuously irregular wax-and-wane patterns of occipito-parietal 10-Hz oscillations have over the past two decades attracted widespread attention in the context of low-dimensional chaos [30, 101, 121]. Chaos theory became mainstream in physics in the early 1980's and contributed with an important insight to the scientific community: chaotic dynamics does not need to have a complicated origin [56]. In fact, certain nonlinear dynamical systems of merely three degrees of freedom can be made to exhibit chaotic behavior in which the state of the system, as defined by the values of the three time-dependent parameters, never

repeats itself [99] (p. 7). A classic example is the forced damped pendulum, which is mathematically straightforward to describe and subsequently can be analyzed analytically and numerically. Much insight has been obtained about the route to chaos through the adjustment of parameters in such simple systems. However, the sensitivity of the dynamics to the accuracy of the parameter values makes it experimentally tedious to generate truly chaotic behavior in experimental settings. Alternatively, a huge number of potential degrees of freedom can undergo a dimensional reduction for narrowly defined parameter settings, such as in Rayleigh-Benard convection where fluids spontaneously form an ordered flow at certain temperature differences between the upper and lower boundaries of the container [69].

The conclusions from the many chaos analyses of human EEG signals have, however, been rather bleak: chaos in terms of a low-dimensional process is presumably more a sign of pathology than a general characteristic feature of the normal alpha rhythm [7, 76].

One may think of various explanations for the unsuccessful outcome of the many attempts to pin-point low-dimensional chaos in alpha oscillations. First, the involved networks consist of millions of neurons and are therefore not low-dimensional *per se*, like, e.g., the forced damped pendulum. Second, if large-scale synchronized activity would emerge, following an analogous path as the formation of ordered flow in Rayleigh-Benard convection, some mechanism in the brain would have to fine-tune essential parameters (often termed "control parameters" [69]) governing the dynamics of the large populations of neurons participating in network oscillations at around 10 Hz. It is, however, far from clear even theoretically what such delicate control mechanisms would be.

The possibility that the intermittent amplitude fluctuations of certain network oscillations should be conceived as the dynamic fingerprint of a high-dimensional process, which is not necessarily chaotic, is treated in Section 3.4.2.

3.4 Self-organization and complexity

The aim of the science of self-organization and complexity is to understand the source and character of structures and temporal dynamics in systems that naturally exhibit large variability. In addition, when applied to biological systems, the aim is to gain insight into the functional implications of spatiotemporal complexity. Finally, one may wish to develop methods that can predict and/or control the evolution of such systems.

A system is said to be *self-organized* when its structure emerges without explicit pressure or involvement from outside the system, i.e., the constraints on the organization result from the interactions among the components and are internal to the system [84]. *Complexity* does not have a strict definition, but a lot of work on complexity centers around statistical power laws, which describe the scaling properties of fractal processes and structures that are common among systems that at least qualitatively are considered complex. The success of describing self-similar fluctuations in time and space with fractal geometry, i.e., in terms of power-law scaling exponents, does, however, not in itself reveal why fractals are ubiquitous in nature. The theory of self-organized criticality (SOC), on the other hand, provides deep insight into this question.

3.4.1 Self-organized criticality (SOC)

The concept of self-organized criticality was originally introduced by Bak, Tang, and Wiesenfeld as a generic mechanism for producing $1/f$ noise [8, 9] and for explaining the widespread occurrence of fractal structures in nature. The core discovery was that self-similar patterns in time and space are a consequence of each other [89].

Bak *et al.* used the agent-based modeling approach (cf. Section 2.4) to simulate the emerging large-scale dynamics of avalanches when grains of sand were added slowly and randomly to a sandpile [8, 9]. The term *self-organized* was coined because a power-law relationship between the size and the frequency of avalanches appeared without any external guidance

other than randomly dropping grains of sand. The term *criticality* was chosen on the basis of the analogy with the dynamics of equilibrium systems near the *critical point* of a phase transition, where domains of different phases of a substance (e.g., ordered vs. disordered magnetic spins) appear in all sizes and with long-range power-law correlations in space and time. Although this dynamics is similar to that of the sandpile, there is a dramatic difference in that critical dynamics in equilibrium systems only appear through the fine-tuning of some parameter (e.g., temperature), while the sandpile self-organize naturally to the critical point.

Motivated by the simplicity of the mechanistic rules in their simulation and the robustness of their results, it was conjectured that SOC is *the* underlying mechanism of scale-invariance in nature. This cannot be ruled out [84], but for obvious reasons it is difficult to prove and also depend on the exact definition of what constitutes SOC [45]. Dynamical systems/processes that so far have been linked to SOC through a combination of empirical power-law statistics and agent-based modeling include earthquakes [13], forest fires [87], financial markets [85,88], avalanches in rice piles [46], epidemics [111], macroscopic evolution [89, 100], and neuronal activity [67, 78]. These and more examples have been reviewed in a couple of excellent books [12, 27].

To understand the essential physics of the self-organization process that drives systems naturally to the critical state, one has to understand how non-randomness emerges from random initial conditions and random input (the driving force). Consider a simple model of forest fires with just two opposing mechanisms: trees are planted at random on a large grid of potential tree locations while lightning strikes also at random [87]. When a tree is hit by lightning, a fire is initiated which propagates to its nearest-neighboring trees. To begin with, the amount of trees that burn down must clearly be random, since neighboring sites are occupied by trees only by chance, but as time goes by regions that have not been ignited by lightning become linked into growing clusters by the newly planted trees. This way, spatial correlations between wide-apart trees emerge, which materializes as a large fire once a tree somewhere in the cluster is set on fire. After such a large fire, trees have vanished which prevents fires in the near future to propagate through that area. As this process goes on for a long time, the amount of and density of trees in larger and larger areas become correlated through the history of fires further and further back in time until the state of every site of the grid (tree or not a tree) depends on in principle past fire activity in every other site. In short, the scale-free spatial and temporal structures emerge hand-in-hand as a natural consequence of the growing correlations via emerging structures (clusters of trees) that in turn bias the path of the temporal dynamics (fires) etc. until the system is fully correlated in a statistical sense.

What counts in the critical state are not complex details, but simple underlying features of geometry that control how influences propagate [27] (p. 92). This is why such a simple model can actually capture the essential physics and reproduce the empirical power-law statistics of wild-forest fires [87].

Put in general terms, the following features are characteristic of SOC systems or vice versa: systems that meet the criteria below are apt to exhibit SOC:

1. Spatially extended
2. Units interact locally
3. Driven slowly
4. Dissipative (or nonlinear)
5. Activity propagates in avalanches
6. Plastic (i.e., amenable to modifications)
7. Insensitive to initial conditions

8. Statistics are robust to random perturbations
9. "Old" (i.e., evolved for a long time relative to its size)

and the critical state is expressed in terms of:

1. Finite-size effects
2. Long-range correlations in space
3. Long-range correlations in time
4. Power-law scaling behavior
5. Criticality: high susceptibility to perturbations

How these general prerequisites of SOC systems apply to neuronal networks, is considered in the following Section (3.4.2).

3.4.2 SOC in large-scale neuronal activity?

A core hypothesis of the present Thesis is that spontaneous oscillations may exhibit self-organized criticality. Here the equivalence of the SOC prerequisites listed in the previous Section (3.4.1) and mechanisms of large-scale neuronal activity is established.

The ideal SOC system is spatially extended with locally interacting units. These features are clearly met by the brain with its typical density of neurons reaching approximately a 10^5 neurons pr. mm^2 of cortical tissue and on the order of 10^3–10^4 synaptic connections pr. neuron [98]. Although many neurons project to distant brain regions, most synaptic connections are made within the macrocolumn of approximately 3 mm in radius [98]. The prerequisite of being spatially extended (i.e., having many units) has to do with the need of the system to generate spatial structures that can hold a memory of past activity. The concept of memory in neuroscience and complexity physics differs a bit. In cognitive neuroscience, memory often has the connotation of a neuronal representation of a previous event that is accessible to the consciousness. In physics or physiology, it has the meaning of a temporal correlation: if the realization of some process is not independent of a previous process, some information about the former process must be stored somewhere, i.e., in space (time is not a "medium" for information storage). This is why structural changes must take place also when the brain encodes consciously accessible memories, e.g., by establishing new synapses or adjusting the efficacy of already existing synapses in an activity-dependent manner [70].

SOC systems are driven slowly, which is of course a relative term. In the forest-fire example (Section 3.4.1) it means that there has to be a reasonable trade-off between the speed of planting trees and the frequency of lightning. This is the logic: if trees are planted very quickly relative to the frequency of lightning, every site becomes correlated with every other site and all fires will be large. Conversely, a very high rate of lightning opposes the formation of large clusters of trees and all fires will be small so that long-range spatial correlations are not allowed to form. Critical behavior is found for ratios in between these extremes. In terms of neurons and neuronal networks, a high driving force could, e.g., be such a high rate of afferent signals that synaptic vesicles would deplete and drive the network into a state of refractoriness with very limited possibilities for neuronal signals to propagate.

The dissipation of energy refers to the need for a nonlinear component for energy or stress to build up, which is then occasionally dissipated via a so-called avalanche effect where activity propagates over large areas via nearest-neighbor interactions. The threshold nature of neurons is clearly nonlinear, e.g., a certain amount of spatial and/or temporal summation of postsynaptic potentials is required for a neuron to generate action potentials. Although, not expressed as an avalanche effect, there are several examples that neuronal activity spreads in this way, e.g.:

"The spontaneous appearance of synchronized oscillations results from the initiation by one or a small number of cells followed by the progressive recruitment of large numbers of neighboring neurons into the synchronized network activity." [14].

Or:

"Propagating neural activity in the developing mammalian retina is required for the normal patterning of retinothalamic connections. This activity exhibits a complex spatiotemporal pattern of initiation, propagation, and termination" [28].

This last quote as well as the comments on neuronal ontogeny in Section 3.1 indicate that neuronal networks are certainly amenable to modifications. In fact, the process of the forest becoming "activated" at random (by lightning), while "remembering" through the creation of spatial patterns of burned forest, may not be so far from that taking place during the early stages of neuronal development when only few synaptic connections have been made and most of the activity correspondingly is largely uncorrelated [144].

An SOC system may develop to the same statistical state irrespective of the initial conditions and a wide range of random perturbations throughout its development, i.e., the critical state is a spatiotemporal attractor of its dynamics [89,100]. Here the argument for a neuronal equivalence has to be more qualitative, since little is known about the statistics of the brain's spatiotemporal organization. Nevertheless, adult human brains are characterized by a high degree of functional and macro-anatomical similarity, despite large variations in the environments in which these brains develop. The differences at the level of cellular morphologies and spines have an almost infinite potential and possibly host the neuronal correlates of many aspects of intersubject variability. Note that a stable statistics for the spatiotemporal organization imposes only weak constraints at the level of the smallest units in a high-dimensional system (like the brain or SOC systems in general).

Finally, the system must be old in order to be in a self-organized critical state, i.e., it must have evolved for a long time relative to its size because the correlations in space and time develop slowly and the system is only truly critical when fully correlated according to statistical power laws. For some SOC systems it has been possible to derive equations for the asymptotic convergence to the critical state as a function of time [100]. This also explains why SOC systems exhibit finite-size effects, i.e., there are cutoffs where the power-law scaling behavior breaks down. The spatial correlations cannot exceed the size of the system and the smallness of the system defines an upper limit to how long temporal correlations the system can hold, because eventually all the structures that were created by some event have been "overwritten". These characteristics must inevitably also hold for neuronal systems, and one may speculate that the longer time it takes for species with larger brains to mature, has to do with mature brains being characterized by a high degree of integrity such as the one signified by power laws and thus requiring longer time to become fully spatially correlated.

SOC systems are not only "critical" in the sense of having power-law correlations in space and time as explained in Section 3.4.1, but also in terms of exhibiting high susceptibility to perturbations, which is also a characteristic of equilibrium systems at the critical point of a phase transition. Qualitatively, neuronal systems may definitely also be considered highly susceptible to perturbations, since quick and reliable responsiveness to incoming signals is a prerequisite for the information processing in the brain.

The evidence that neuronal structures should exhibit SOC is currently limited to a couple of reports. Jung *et al.* observed power-law scaling behavior in the spatiotemporal organization of calcium waves in a culture of glial cells [67] and in a computational model of the same system [66]. Simulations of neuronal populations that generate dynamic patterns or traveling waves, which translate into $1/f$ noise, have been reported by Usher *et al.* [141]

and Chialvo *et al.* [34]. Interestingly, these results did not depend on a long refractory time and therefore showed that long-memory effects can emerge as a network property. In the macroscopic human EEG, power-law scaling behavior has been reported for the duration of bursts of oscillations [51] and for their temporal correlations [78].

3.5 Stochastic resonance

Stochastic resonance (SR) is a phenomenon where a weak signal is detected or transmitted optimally in the presence of noise. This paradoxical increase of output signal-to-noise ratio has been demonstrated in several systems including lasers, semiconductor devices, chemical reactions, and physiological mechanoreceptors [49, 147]. The basic prerequisite for a system to exhibit stochastic resonance is a threshold that needs to be exceeded in order to activate the system. When the signal in itself is not strong enough to exceed the threshold, small amounts of noise added either to the system or the signal may occasionally suffice to trigger activation, therefore the term *stochastic resonance* [49].

3.5.1 Stochastic resonance in neuronal activity

Stochastic resonance in neuronal systems is well established both experimentally [42, 90, 114] and theoretically [36, 120] through controlled addition of external noise. The noise is often added to the signal, which has been shown to improve, e.g., the ability of paddle fish to detect prey [114], human visual perception [117], somatosensation [37], and the speed of memory retrieval [142].

Although stochastic resonance due to interactions between a signal and a noisy environment is interesting, it does not enable a physiological system to exploit stochastic-resonance effects actively by controlling the level of noise. The possibility that the endogenous activity of physiological systems may play the role of "noise" for stochastic-resonance-based processing of neuronal signals has been suggested by several investigators [15, 26, 32, 36, 42, 55, 69, 97, 120, 137], but evidence for this so-called intrinsic stochastic resonance has only been obtained from simulation studies [35, 113, 120, 128, 129].

The impact of background activity on neuronal responsiveness was recently investigated in morphologically reconstructed pyramidal cells [61]. The influence of membrane-voltage fluctuations was highlighted as an important contributing factor, having a stochastic-resonance relationship for the probability of evoking a spike to input that was subthreshold in the absence of background activity. This finding is in line with previous proposals [82], and suggests that certain levels of spontaneous or ongoing activity in neuronal networks may serve the function to facilitate information transmission through a mechanism of intrinsic stochastic resonance [61].

4 Aims of Study

The overall aim of the studies in this Thesis has been to understand the state of the human brain during wakeful rest and how this state is affected by and affects the processing of incoming information from our sensory environment. To this end, the sensorimotor system was chosen as the primary model system and 10- and 20-Hz oscillations as indices of the brain states.

The main aims of the six studies were:

P1:
To find evidence for self-organized criticality in ongoing oscillatory activity.

P2:
To characterize the influence of ongoing oscillations on somatosensory evoked fields.

P3:
To characterize the single-trial reactivity of ongoing oscillations to somatosensory stimulation.

P4:
To characterize interhemispheric phase synchrony and amplitude correlations of ongoing oscillations.

P5:
To probe the stability of long-range power-law temporal correlations of ongoing oscillatory activity during sensory-induced perturbations.

P6:
To show that ongoing oscillations may facilitate the processing of weak somatic stimuli in a manner that is consistent with a mechanism of intrinsic stochastic resonance.

5 Materials and Methods

The empirical data of the present studies (P1–P6) were obtained with non-invasive recordings of electrical activity in normal human subjects using multi-channel electroencephalography (EEG) and/or magnetoencephalography (MEG). The EEG cap, covering the entire scalp, had 64 electrodes [146], while the helmet-shaped sensor array of the MEG contained either 122 or 306 SQUID sensors [72]. For the present studies, a subset of typically 2–4 channels (based on anatomical location and high signal-to-noise ratio) was chosen for the detailed analysis.

Electrical somatosensory stimulation was used in P2, P3, P5, and P6. Constant-current pulses of 0.2-ms duration were applied either to the median nerve with the strength adjusted above the motor threshold for the abductor pollicis brevis (P2, P3, and P5) or to the tip of the index fingers with the strength adjusted approximately to the 50%-detection threshold (P6). Conditions of wakeful rest without sensory stimulation were used in P1, P4, and P5.

Wavelet filtering was used in all studies to estimate the amplitude and phase of a given oscillation with high resolution in time and frequency domain [136]. More technical details regarding the properties of this filter are given in P5.

Temporal correlation analysis of long time series (20 min) of the oscillation-amplitude envelope was used extensively (P1 and P5) and was based on three complementary methods: power spectral density, autocorrelation, and detrended fluctuation analysis.

The power spectral density of the signals was determined by means of the Welch technique with the Hanning window; it reveals the contribution of different frequencies to the total power of the signal. White-noise signals contain equal power at all frequencies and are usually considered uncorrelated, while long-range correlated signals often have log-log linear power spectra with a non-zero power-law exponent ($1/f^{\beta}$ signal). Periodic signals have peaks in the spectrum at frequencies corresponding to the inverses of these periods. The important difference between a power spectrum of the recorded broadband signal (e.g., 0.1–100 Hz) and the amplitude envelope of narrow-band neuronal oscillations (e.g., 7–13 Hz), is shown in Fig. 2.

The autocorrelation function gives a measure of how a signal is correlated with itself over different time lags. A normalized autocorrelation function attains its maximum value of one at zero time lag, decays towards zero with increasing time lag for finite correlated signals, and fluctuates close to zero at time lags free of correlations. Signals that are modulated at a characteristic scale produce autocorrelation functions that are also modulated with the period of the characteristic scale.

The detrended fluctuation analysis has been developed for quantifying correlations in non-stationary signals, e.g., in physiological time series, because long-range correlations—revealed by the autocorrelation function—can arise also as an artifact of the "patchiness" of non-stationary data [104]. The detrended fluctuation analysis measures the variance of linearly detrended signals, $F(\tau)$, as a function of window size, τ, (for graphical details, see Fig. 1 in P1). The average fluctuation, $\langle F(\tau)\rangle$, is often of a power-law form:

$$\langle F(\tau)\rangle \approx \tau^{\alpha} \tag{2}$$

The scaling exponent α is extracted with linear regression in double-logarithmic coordinates using a least-squares algorithm. An exponent of $\alpha = 0.5$ characterizes the ideal case of an uncorrelated signal, whereas $0.5 < \alpha < 1.0$ indicate power-law scaling behavior and the presence of temporal correlations over the range of τ where relation (2) is valid. Periodic signals have $\alpha = 0$ for time scales larger than the period of repetition.

The above three complementary tests were used because of recent reports pointing out that one of these methods used alone may indicate the presence of long-range correlations as an artifact of the patchiness of non-stationary data [104], while agreement between independently obtained scaling exponents according to theoretically derived relationships lowers

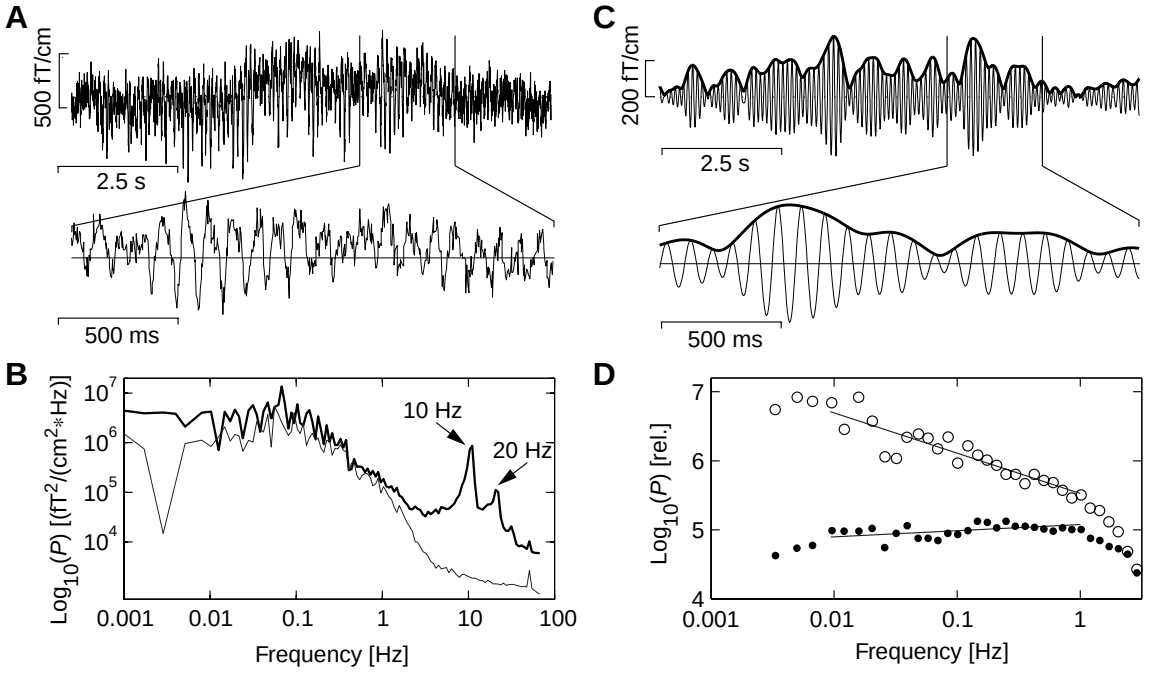

Figure 2: The frequency content of broadband signals and of the amplitude envelope of narrow-frequency-band neural oscillations. *A*, A representative epoch of the broadband signal as obtained from a single MEG channel at the acquisition (0.1–100 Hz) is shown at two time scales. Note from the *upper trace* that the high-amplitude 10-Hz oscillations are riding on slow fluctuations (< 1 Hz). The slow fluctuations in the broadband signals are likely to originate mainly from environmental noise as it can be inferred from *B* showing the spectral density of the entire 20-min long signal in *A* (*thick line*) and reference data from the same channel (*thin line*). The neural signals clearly dominate at frequencies above but not below 1 Hz with prominent peaks at 10 and 20 Hz (see *arrows*). *C*, The signal shown in *A* has been filtered at 10 Hz with a Morlet wavelet (passband 6.7–13.3 Hz). The *thin lines* are the real part and the amplitude envelopes (*thick lines*) are the modulus of the wavelet transform. *D*, The power spectrum of the amplitude envelope of the neural data at 10 Hz exhibits a $1/f^{\beta}$ power spectrum (*circles*) with $\beta = 0.58$ in the range from 0.01–1 Hz, thereby indicating that the fluctuations of the amplitude envelope of these oscillations are correlated at time scales of 1–100 s. On the contrary, the 10-Hz amplitude envelope of the reference data gave rise to a white-noise spectrum characteristic of a temporally uncorrelated process (*dots*). Note that all the analyses of temporal correlation reported in the Thesis were performed on the amplitude *envelope* of oscillatory activity (*thick lines* in *C*).

the risk of falsely concluding that a given data set contain long-range correlations [110].

In P4, we used the recently developed synchronization index based on wavelet transformation for the evaluation of synchrony, instead of the more traditional coherence function, which suffers from the drawback that it is a confound measure of phase and amplitude and can give rise to an overestimation of the actual phase coupling [132]. The synchronization index, S, is given by:

$$S = \frac{1}{N} \mid \sum_{t=1}^{N} e^{j\theta(t)} \mid \tag{3}$$

where N is the number of samples in the time series, j is the imaginary unit, and θ is the phase difference between the two signals. S attains the value 1 for perfectly synchronized signals and 0 for infinite amount data that are not synchronized [74].

The experimental paradigm of each study is described in the "summary of publications" in Sections 6.1–6.6.

6 Summary of publications

This Thesis is based on six publications, which are summarized below (Sections 6.1–6.6).

6.1 Long-range temporal correlations and scaling behavior (P1)

The human brain spontaneously generates neuronal oscillations with a large variability in frequency, amplitude, duration, and recurrence. Little, however, is known about the long-term spatio-temporal structure of these complexly fluctuating oscillations. We hypothesized that ongoing oscillations may self-organize to a critical state, which is characterized by large variability and long-range temporal correlations of a power-law form and similar to that of other stochastic multi-unit systems (cf. Section 3.4.1 and 3.4.2).

We investigated the temporal structure of 10- and 20-Hz oscillations in the normal human brain at time scales ranging from a few seconds to several minutes. Ongoing activity during eyes-open and eyes-closed conditions was recorded from 10 normal subjects with simultaneous magnetoencephalography (MEG) and electroencephalography (EEG).

Highly irregular fluctuations of the amplitude envelope of the oscillations at around 10 and 20 Hz were observed in both conditions over the occipito-parietal region (Fig. 3*A*,*B*). A linear decay of power with increasing frequency in double-logarithmic coordinates was observed in the range of 0.005–0.5 Hz for both MEG and EEG data and the conditions of eyes open and eyes closed, indicating a $1/f^{\beta}$ type of a power spectrum and thus a lack of a characteristic time scale for the duration and recurrence of these oscillations (Fig. 4*A*). The autocorrelation analysis indicated the presence of statistically significant correlations up to time lags of more than a hundred seconds (Fig. 4*B*). The decay of the autocorrelation function was slow over two decades and well fitted by a power law, which is in congruence with the $1/f^{\beta}$ power spectra.

To further consolidate the presence of long-range correlations, we implemented the detrended fluctuation analysis (DFA) [103,104]. The self-similarity parameter, α, of the DFA is the power-law exponent characterizing the temporal correlations; uncorrelated signals yield a self-similarity parameter $\alpha = 0.5$. The lack of temporal correlations in the reference recording and surrogate EEG data was confirmed, while the 10-Hz oscillations exhibited robust power-law scaling behavior across conditions (Fig. 4*C*).

Altogether, these results indicate that the irregular amplitude fluctuations of occipito-parietal 10-Hz oscillations (Fig. 3) are embedded with correlations at many time scales and that the decrease in correlation with temporal distance is governed by a power law (Fig. 4).

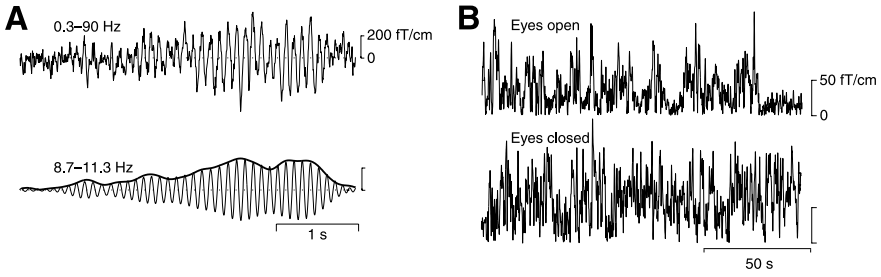

Figure 3: 10-Hz oscillations dominate the ongoing activity and fluctuate in amplitude on a wide range of time scales. *A*, MEG signal from the occipito-parietal region in the eyes open condition. The 4-s epoch of broadband activity (0.3–90 Hz, *upper curve*) displays a typical transition from small- to large-amplitude 10-Hz oscillations. The thick line of the *lower curve* indicates the amplitude envelope of the bandpass-filtered signal (8.7–11.3 Hz) obtained with the wavelet filter. *B*, Intermittent fluctuations in the 10-Hz-oscillation amplitude are seen in 150-s epochs from conditions of eyes open (*upper curve*) and eyes closed (*lower curve*).

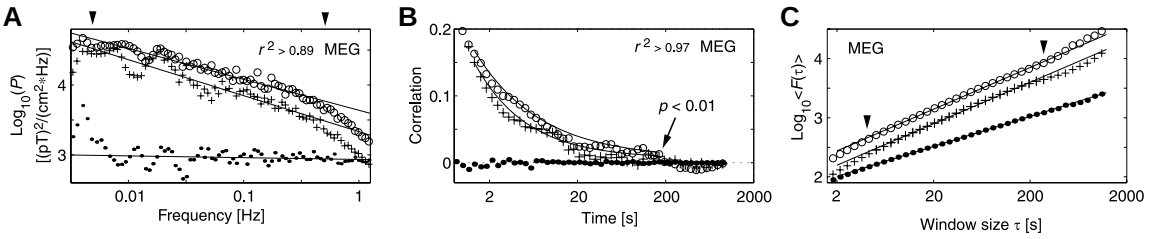

Figure 4: Occipito-parietal 10-Hz oscillations exhibit long-range temporal correlations and power-law scaling behavior for their amplitude modulation. *A*, The grand-averaged power spectral density of 10-Hz-oscillation amplitude fluctuations is plotted in double-logarithmic coordinates for the MEG data. *Circles*, eyes closed condition; *Crosses*, eyes open. The *dots* represent an empty-room reference recording. *B*, The autocorrelation functions exhibit a power-law decrease in correlation with increasing time lag. The abscissas are logarithmic and the solid lines are power-law fits to the data. Significant correlations were obtained at time lags of nearly 200 s for the brain data. *C*, Double-logarithmic plots of the DFA fluctuation measure, $F(\tau)$, show power-law scaling in the time-window range of 5 to 300 s.

Moreover, we did not find differences in scaling exponents between the two conditions or between the MEG and EEG recordings.

Previous studies, aimed at understanding the irregular nature of ongoing 10-Hz oscillations, have usually hypothesized a low-dimensional chaotic process and analyzed short data segments (< 10 s) [30, 101, 121]. The evidence for chaos has, however, not been robust and also left unknown to what extent oscillatory activity is statistically dependent beyond the time scale of about 10 s. The present scaling analyses indicate that successive oscillations indeed are correlated—even over thousands of oscillation cycles.

We propose that the large variability, the long-range correlations, and the power-law scaling behavior of ongoing oscillations find a unifying explanation within the theory of self-organized criticality, because of the correspondence between the physiological properties of neuronal networks generating ongoing oscillations and the general mechanisms of SOC (cf. Section 3.4.1 and 3.4.2).

From a theoretical point of view and based on simulations, it has been argued that a state of criticality would be optimal for a network to swiftly adapt to new situations [3,33,123]. In line with these studies, we further suggest that critical-state dynamics of ongoing oscillations may lend neuronal networks capable of quick re-organization during processing demands.

6.2 Pre-stimulus oscillations and somatosensory evoked fields (P2)

In the present study, we examined whether somatosensory evoked fields depend on the state of the sensorimotor cortex as indexed by the pre-stimulus amplitude of 10-Hz oscillations.

Somatosensory evoked magnetic field components N20m, P35m, and P60m in response to median nerve stimulation were selectively averaged into five groups on the basis of the amplitude of ongoing 10-Hz oscillations in different pre-stimulus-window sizes (380, 480, and 980 ms). In each subject, amplitudes of the evoked components were determined from the MEG channel showing the maximum amplitude for each deflection over the contralateral somatosensory cortex; 10-Hz-oscillation amplitudes were taken from the same channels as the somatosensory evoked fields (Fig. 5).

The N20m somatosensory evoked field deflection did not depend on pre-stimulus activity, while the amplitude of the P35m deflection, and to a lesser extent that of the P60m deflection, showed a small positive correlation with the amplitude of the pre-stimulus activity (Wilcoxon Matched Pairs Test, Fig. 6). These results were not very sensitive to the choice of pre-stimulus window size. Although the amplitude of the 10-Hz oscillations varied by 230–500%, the maximum variations in P35m and P60m amplitudes were only 21 and 12%, respectively. Thus, the results indicate a remarkable stability of the amplitude of somatosensory evoked

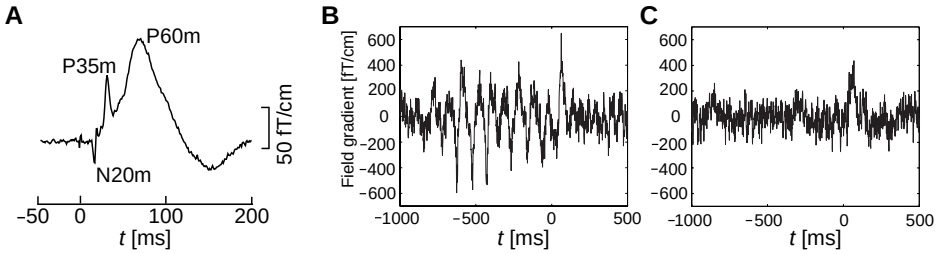

Figure 5: *A*, Somatosensory evoked field from a representative subject with the conventional components indicated. Two single-trial epochs with a 1-s baseline of high and low levels of pre-stimulus activity are displayed in *B* and *C*, respectively.

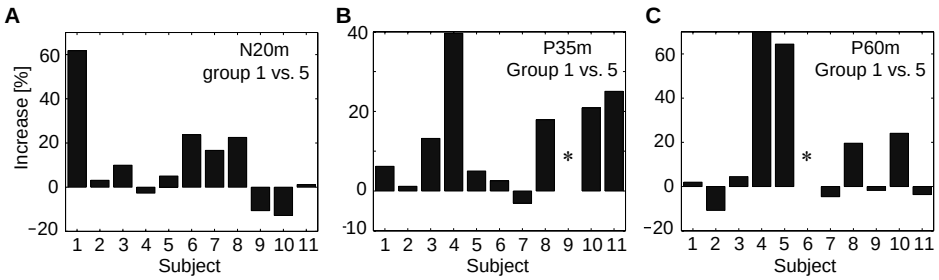

Figure 6: Percentage increase of somatosensory evoked components N20m, P35m, and P60m between the group of trials with lowest and highest pre-stimulus activity are shown for each subject in *A*, *B*, and *C*, respectively. P35m was missing in subject 9 and P60m in subject 6.

components with respect to the pre-stimulus oscillatory state of sensorimotor cortex, but also that the stimulus-evoked processing can be influenced by the level of ongoing activity.

Arieli *et al.* [5] showed that evoked responses in the visual cortex of the anaesthetized cat can be described as a simple summation of the deterministic stimulus-locked response and ongoing cortical activity. Therefore, variability of the evoked potentials in single trials was caused mainly by variability in spontaneous activity. This study would predict that when non-phase locked activity is eliminated (i.e., by averaging) one would get almost deterministic responses. This is in agreement with our study, which shows relative stability of somatosensory evoked fields with respect to variable sensorimotor 10-Hz oscillations.

Finally, we observed stronger increases of P35m and P60m between the first and the fourth group of trials than for the first and fifth group. Although this tendency was not significant it became the source of inspiration for the hypothesis that 10-Hz oscillations produce stochastic resonance in sensorimotor cortex, which we tested later (cf. Section 6.6).

6.3 Reactivity of sensorimotor oscillations to median nerve stimulation (P3)

Somatosensory stimulation is known to attenuate the amplitude of ongoing 10-Hz oscillations in sensorimotor cortex, which is an example of the so-called event-related desynchronization (ERD) [106]. Here we addressed the reliability of ERD across single trials, the lateralization, and the variation as a function of stimulus repetitions in an experimental session, which have remained poorly characterized.

Left and right median nerves were stimulated alternately every 2.2 s with suprathreshold constant-current pulses. An example of 10-Hz oscillations that were attenuated in both hemispheres by median nerve stimulation, but more in the contralateral one is displayed in Fig. 7. Averaged across the subjects, ERD in the contra- and ipsilateral hemispheres was 53 ± 7 and 33 ± 5% (mean ± SEM), respectively, for the stimulation of the left median nerve and 56 ± 7 and 31 ± 6% for the stimulation of the right median nerve. The differences

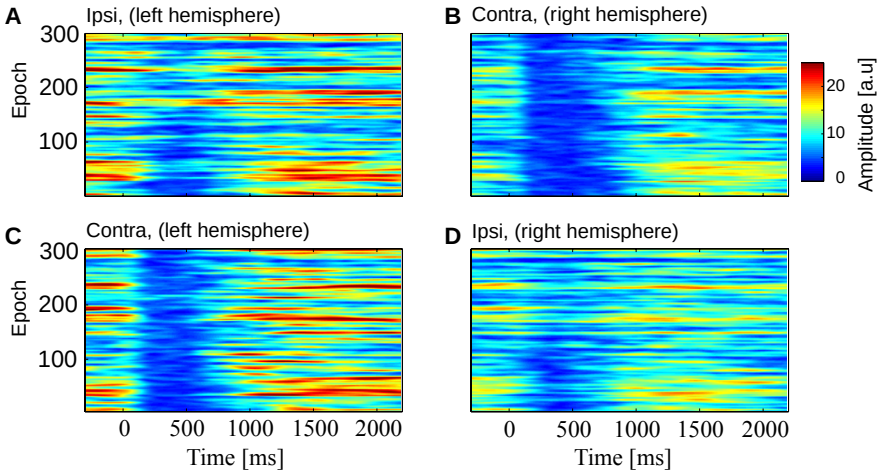

Figure 7: Amplitude attenuation of sensorimotor 10-Hz oscillations in the contra- and in the ipsilateral hemisphere. The amplitude envelope of 10-Hz oscillations is color coded to visualize the single-trial event-related de-synchronization for left median nerve stimulation (A and B), and for right median nerve stimulation (C and D). The amplitude attenuation is robust and bilateral in the beginning of the session, while the attenuation is less prominent in the ipsilateral hemisphere towards the end of the experiment.

between contra- and ipsilateral ERD were significant (Wilcoxon Matched Pairs Test, $p < 0.05$).

In the ipsilateral hemisphere, the ERD became less pronounced in the course of the experiment, which may also be seen from Fig. 7. This effect was significant at the group level ($p < 0.001$ for both hemispheres), while the suppression in the contralateral hemisphere did not attenuate.

The present finding of stable contralateral ERD, together with the fact that contralateral somatosensory components P35m and P60m showed an attenuation while N20m remained stable in the course of the experiment [4, 94] suggest that ERD in the contralateral hemisphere is triggered by the initial thalamic afferent volley rather than by the subsequent somatosensory processing. Moreover, the lateralization of ERD to median nerve stimulation suggests that the strong lemniscal input to the contralateral primary somatosensory cortex has a greater impact on the ongoing oscillations compared to the input to the ipsilateral hemisphere, which is conveyed by transcallosal fibers and/or by extralemniscal subcortical pathways [96].

We have shown that pronounced ERD of 10-Hz oscillations to somatosensory stimuli is observed in the contralateral hemisphere, indicating a high susceptibility of these oscillations presumably to the initial thalamic afferent volley. The ERD in the ipsilateral hemisphere, however, was less strong and attenuated in the course of the experiment.

6.4 Interhemispheric phase synchrony and amplitude correlations (P4)

Neuronal populations may transiently entrain each other also over longer distances [44]. Especially phase synchronization has attracted widespread attention in this context because of the putative functional role of providing a common reference for temporal coding in a distributed network of neurons [47, 57, 119].

In the present study, we investigated interhemispheric phase synchrony and amplitude correlation of ongoing 20-Hz oscillations in left and right sensorimotor cortices during wakeful rest.

The phase-lag distributions revealed statistically significant peaks for the interhemispheric signals in all subjects (above 3 SD of the shuffled data, $p < 0.01$, Fig. 8A), indicating that phase synchrony of 20-Hz oscillations in the left and right hemispheres is a robust

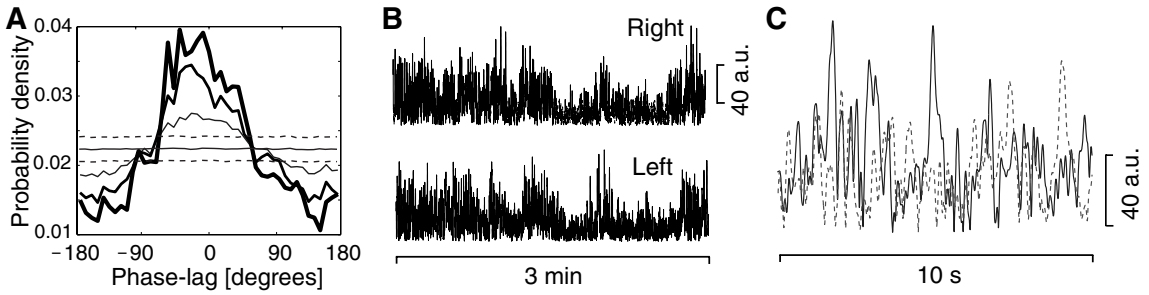

Figure 8: Phase synchrony and low-frequency amplitude correlation between 20-Hz oscillations in the two hemispheres. *A*, Phase-lag distribution for: no amplitude-threshold (*thin line*) calculations, 50 percentile amplitude threshold (*middle thick line*) and 75 percentile amplitude threshold (*thick line*) calculations. The solid horizontal line and the dashed lines represent mean and three standard deviations of 1000 shuffled data sets, respectively. *B*, Similar oscillation-amplitude fluctuations are seen for the right (*upper panel*) and left (*lower panel*) hemispheres on the time scale of minutes, while a representative 10-s epoch (*C*) exhibit very different behavior on short time scales (*dashed* and *solid* line represent left- and right-hemisphere 20-Hz oscillations, respectively.

phenomenon.

Visual inspection revealed that large-amplitude 20-Hz oscillations in one hemisphere could occur when virtually no 20-Hz oscillations were generated in the other. The proper evaluation of synchrony for these segments of time is not possible. The synchronization index was therefore also calculated when the amplitude of 20-Hz oscillations in both hemispheres exceeded the 50 or 75 percentile thresholds. An average increase of the interhemispheric synchronization index of 200% was observed when the 75-percentile amplitude-criterion procedure was applied. Whether this increase was solely due to a signal-to-noise effect or also include a physiologically stronger coupling when two interacting populations of neurons generate high levels of oscillatory activity, these results suggest that one may benefit greatly from amplitude sorting also when interested in phase interactions.

The similarity of the amplitude dynamics of 20-Hz oscillations in the two hemispheres depends to some extent on the time scale of evaluation. The signals look similar on a minute time scale (Fig. 8*B*), whereas on a second time scale the oscillation amplitude shows no clear similarity between the left and right hemispheres (Fig. 8*C*). To quantify this amplitude relationship between the two hemispheres, correlation coefficients were calculated for the wavelet-transformed data with different low-pass-filter settings. The strength of the amplitude correlation increased when lowering the cut-off frequency, reaching the value of 0.58 for 0.1 Hz compared to 0.16 with no filtering. The independence of the oscillatory processes in the two hemispheres on short time scales suggests a considerable degree of freedom for local cortical networks despite externally imposed bias or entrainment, e.g., from the other hemisphere or a subcortical structure. The MEG recordings, however, did not permit to decide whether the observed interhemispheric synchrony or amplitude correlation of 20-Hz oscillations were produced by transcallosal connections [43] or cortico-subcortical mechanisms [91]. The combination of freedom to act locally while retaining global coordination is often considered a hallmark of complex adaptive systems in a critical point or at the "edge of chaos" as this state has often been termed [84].

The involvement of 20-Hz oscillations in different motor tasks has been demonstrated by several investigators [41, 107]. In line with these studies, we propose that the interhemispheric synchrony of spontaneous 20-Hz oscillations may have functional significance for movement organization. If synchrony indeed serves to select and group populations of neurons for further joint processing [119], synchrony between the two motor cortices would be beneficial for the organization of bilateral movements, but may, however, have a negative effect on the organization of unilateral movement. It has been noticed that both contra- and ipsilateral hemispheres are active during the preparation of unilateral movements [73]. One

explanation for the origin of ipsilateral activity is the development of inhibitory processes in the ipsilateral hemisphere, which is related to the suppression of a "mirror" movement of the other hand that are particularly apparent when the level of concentration is weakened [73]. The synchrony between left- and right-hemisphere 20-Hz activity may therefore be utilized for the coordination of bilateral movements, but the payoff for this synchronization can be a need to suppress the "mirror" movements.

6.5 Changes in long-range temporal correlations and scaling behavior (P5)

The discovery of long-range temporal correlations and power-law scaling behavior in the intermittent fluctuations of the amplitude of ongoing oscillations (cf. Section 6.1) suggested that the underlying neuronal networks may self-organize to a critical state. To pursue this idea further, we investigated the effect of electrical somatosensory stimuli on the temporal correlations of the amplitude envelope of 10- and 20-Hz oscillations in sensorimotor and occipito-parietal regions. As neuronal activity evoked and reorganized by somatosensory stimuli modifies the patterns of functional connectivity, we hypothesized that these perturbations degrade the network's ability to hold a memory of ongoing oscillations.

The subjects were in a state of wakeful rest with their eyes closed when we recorded ongoing neuronal activity simultaneously with magnetoencephalography and electroencephalography in two sessions of 20 min. In the stimulation condition, the left median nerve was electrically stimulated every 3 s. In the control condition, no stimulation was applied.

The amplitude and the duration of the bursts of sensorimotor oscillations at around 10 and 20 Hz showed considerable variability both in the control and the stimulation condition (data not shown). Median nerve stimulation, however, induced an immediate but transient amplitude attenuation of the oscillations that was discernable on a single-trial basis (see also Section 6.3). This suggested that sensorimotor oscillations seemingly retain their large amplitude variability across many time scales despite frequent reorganization caused by externally induced perturbations.

We then quantified the temporal correlations of sensorimotor oscillations using three complementary methods: power spectral density (PSD), autocorrelation function (ACF), and detrended fluctuation analysis (DFA). In the control condition, these amplitude fluctuations were characterized by $1/f^{\beta}$ power spectra as reported earlier (cf. Section 6.1). For the stimulation condition, on the other hand, the PSD revealed a highly significant modulation of the amplitude envelope of both 10- and 20-Hz oscillations at 0.33 Hz (Fig. 9*A*), which corresponds to the 3-s stimulation period and the stimulus-induced amplitude attenuation. At frequencies below 0.3 Hz (0.005–0.3 Hz), the power spectra retained their $1/f^{\beta}$ form.

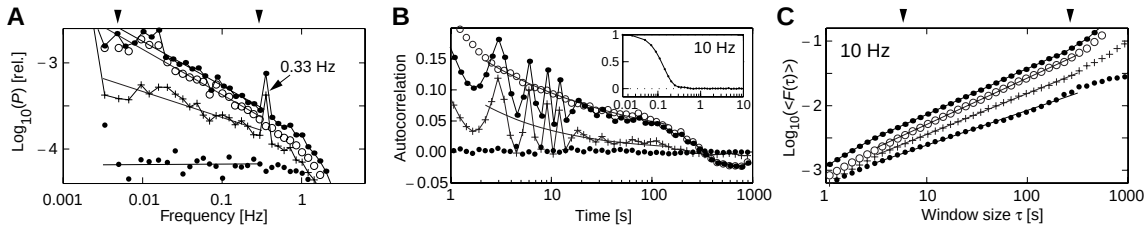

Figure 9: Sensorimotor oscillations exhibit long-range temporal correlations and condition-specific scaling behavior for their amplitude modulation, yet with a characteristic scale during stimulation. The characteristic scale is seen as a sharp increase in power at the frequency of 0.33 Hz (*A*, *Arrow*) and modulation at multiples of 3 s in the autocorrelation function (*B*). *Circles*, control; *crosses*, stimulation. *C*, Condition-specific power-law scaling behavior may be seen from the detrended fluctuation analysis as the difference in slope between control and stimulation. The *connected dots* and the *dots* represent the surrogate data and reference recording, respectively. (The curves in *A* and *C* have been vertically offset for the purpose of visualization). The integration by the wavelet renders the data strongly correlated at time lags shorter than 0.2 s (see inset in *B*).

The power-law exponent, however, for both 10- and 20-Hz oscillations were smaller in the stimulation condition ($p < 0.02$).

Autocorrelation functions and detrended fluctuation analysis also indicated the presence of long-range power-law temporal correlations in both conditions (Fig. 9*B*,*C*), thereby consolidating the PSD analysis. Moreover, the ACF indicated a clear periodic modulation and the DFA scaling exponents were larger in control than in stimulation conditions for both 10 and 20-Hz oscillations ($p < 0.02$). These condition-specific changes in long-range temporal correlations of sensorimotor oscillations were not observed for the occipito-parietal oscillations suggesting that the attenuation of temporal correlations of the sensorimotor 10- and 20-Hz oscillations was mediated by activity induced by the somatosensory stimuli, rather than more general changes in brain states [60].

Finally, we generated surrogate data by computing the event-related percentage change in 10-Hz-oscillation amplitude (as a function of time) for each individual subject and subsequently used these time-dependent coefficients to artificially introduce periodic modulations of the amplitude time series of the control condition. Interestingly, we did not find differences in the power-law exponents between the surrogate and the control, but between the surrogate and stimulation data in the PSD. Also on the basis of the DFA scaling exponents, we observed no evidence that the periodic modulation per se could explain the attenuation of long-range temporal correlations, since the difference between stimulation and surrogate data was significantly larger than the difference between control and surrogate data ($p < 0.001$).

The population oscillations studied here are likely to induce changes in the functional connectivity when propagating through the cortical networks and thereby leave behind a physiological memory trace that affects the future recruitment of neurons. We suggest that neuronal activity evoked and reorganized by sensory stimuli disrupts the evolution of these intricate and transient patterns of connectivity and thereby leads to an attenuation of temporal correlations and changed scaling behavior.

Our results point to a dual role for the critical-state dynamics in neuronal network oscillations. A critical state endows the neuronal networks with a high susceptibility to processing demands and yet allows for the preservation of the critical state in the presence of these perturbations (Fig. 9). Interestingly, it was recently shown in a neural network simulation that $1/f$-noise is superior to brown and white noise in optimizing stochastic resonance [97]. Thus, the stability of the dynamic state of the ongoing oscillations may be important if the brain were to exploit intrinsic stochastic resonance—an information-transmission phenomenon that produces optimal signal detection at some nonzero level of endogenous noise [61], which we tested in Section 6.6.

In conclusion, we have shown that local stimulus-induced perturbations of ongoing oscillations degrade but do not abolish a neuronal network's memory of its past. Furthermore, we have demonstrated that power-law scaling exponents can be valuable indices for the characterization of the intermittent amplitude fluctuations of network oscillations across many time scales and how this dynamics may change with experimental conditions.

6.6 Intrinsic stochastic resonance mediated by ongoing oscillations (P6)

Theoretical studies have indicated that a certain level of "intrinsic noise" may improve the ability of a neuronal system to detect and transmit weak signals through a mechanism of so-called intrinsic stochastic resonance [113, 120, 128]. To test this possibility in humans, we hypothesized that intermediate levels of ongoing oscillatory activity of the sensorimotor cortex—often considered "idling rhythms" [93]—may serve as a beneficial type of "endogenous noise" for the processing of weak somatic stimuli.

We quantified the relationship between pre-stimulus oscillation amplitude and (*i*) the hit rate of stimulus detection and (*ii*) the reaction time. The subjects ($n = 14$) were stimulated

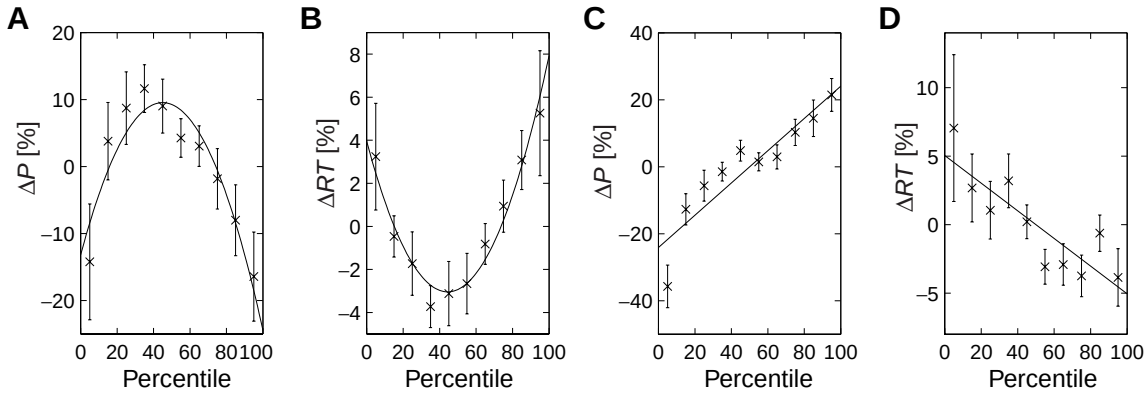

Figure 10: Evidence for intrinsic stochastic resonance in the psychophysical performance. The hit rates and reaction times of consciously detecting the weak somatosensory stimuli have been sorted into bins of 10-percentile steps with respect to the contralateral pre-stimulus 10-Hz-oscillation amplitude. The difference in probability of detection (ΔP) (A) and the difference in reaction time (ΔRT) (B) relative to the individual means exhibit a clear extremum at intermediate amplitude levels of the ongoing oscillations (grand-average mean ± SEM). The non-linear relationship between oscillation-amplitude and psychophysical performance has a strong quadratic component as indicated by the least-squares fits to the data (solid lines). The occipito-parietal 10-Hz oscillations, however, do not induce stochastic resonance in the psychophysical performance. The difference in probability of detection (ΔP) (C) and the difference in reaction time (ΔRT) (D) relative to the individual means are monotonously increasing functions of the amplitude of the occipito-parietal 10-Hz oscillations (grand-average mean ± SEM).

with weak electric pulses to the left and/or right index finger and indicated the perception of the stimuli with a prompt twitch of the thumb of the stimulated hand. During the experimental sessions, subjects were sitting relaxed with their eyes closed while their neuronal activity was recorded with whole-scalp magnetoencephalography.

The average performance was characterized by hit rates of 32 ± 13% (mean ± SD) and reaction times of 498 ± 82 ms. Sorting the hit rate into bins in steps of 10 percentiles with respect to the mean pre-stimulus 10-Hz-oscillation amplitude in a 1000-ms window in contralateral sensorimotor cortex, however, revealed a higher reliability of consciously perceiving the weak electric stimuli at *intermediate* than at low or high levels of activity (Fig. 10A). Fitting linear and quadratic functions clearly indicated a nonlinear relationship between the hit rates and the pre-stimulus activity (linear regression: $R^2 = 0.12$, $P = 0.33$; quadratic $R^2 = 0.88$, $P < 0.001$). Functionally, the pre-stimulus dependence was remarkably significant: hit rates improved by an average of 25% at optimal levels of pre-stimulus activity compared to the extreme low or high levels.

A non-monotonic correlation was also revealed between the pre-stimulus activity and the reaction time of the detected trials: subjects responded on average 7–8% faster at intermediate amplitudes of pre-stimulus oscillations compared to the extreme high or low levels (linear regression: $R^2 = 0.16$, $P = 0.26$; quadratic: $R^2 = 0.96$, $P < 0.0001$, Fig. 10B). In sharp contrast with these parabola-shaped curves, a strong linear correlation was observed between hit rates and reaction times when sorting with respect to the occipito-parietal 10-Hz oscillations (linear regression: $R^2 > 0.73$, $P < 0.001$, Fig. 10C,D).

We have demonstrated that the pre-stimulus amplitude of ongoing sensorimotor oscillations of the human brain correlates with the reliability and speed of detecting weak somatosensory stimuli in a nonlinear fashion that is consistent with a mechanism of intrinsic stochastic resonance. Several previous studies have shown that the addition of external noise to either signal [37,77,90,117,130] or neuronal systems [26,36,39,42,97,128,142] can enhance the output signal-to-noise ratio of detecting weak input signals. Our results provide the first empirical evidence that the human central nervous system may have evolved to exploit its endogenous activity for signal detection and information transfer as it has been proposed

by several investigators [15, 26, 36, 42, 55, 69, 97, 120, 137]. Intrinsic stochastic resonance may provide a useful framework for understanding the functional significance of so-called "idling rhythms" in several cortical areas, e.g., the rebound of these oscillations shortly after a stimulus-induced amplitude attenuation [108] may serve to quickly bring the network back into the more optimal oscillatory state.

7 General discussion

This Thesis has aimed at improving our understanding of the dynamic nature and functional significance of oscillatory activity in the human brain. Most of the present studies have relied on the analysis of 10- and 20-Hz oscillations in the sensorimotor region. It is expected, however, that most of the results can be generalized to similar oscillations in other areas of the brain. In particular, I would expect network oscillations at around 10 Hz in other primary sensory areas to also exhibit power-law decay of temporal correlations and give rise to stochastic-resonance like phenomena. On the other hand, it remains an open question to what extent the power-law temporal correlations may generalize, e.g., to other conditions than those tested here, to other species, or to oscillations in the delta-, theta-, or gamma-frequency ranges which presumably are generated through different cellular mechanisms.

Ongoing oscillations tend to emerge in primary sensory areas during wakeful rest and are therefore widely known as idling rhythms [59]. The present results may both be viewed as supporting and extending the idling hypothesis, because SOC dynamics is expected especially during inactivity or modest levels of imposed processing demands, so the "idling" term seems in place. The high susceptibility to imposed processing demands (cf. P3, P5, and P6) may be taken as an indication—albeit indirect—that idling rhythms play a role in the processing of information in the brain [82]—they at least exhibit reactivity. A mechanism of stochastic resonance between the level of oscillatory activity and afferent signals as suggested by the findings in P6, however, provide a stronger indication that the resting state oscillations serve a function related to stimulus processing. The stochastic-resonance relationships also provide a functional logic to the phenomenon of event-related synchronization or "rebound", e.g., of sensorimotor oscillations [108]. The return of the ongoing oscillations to levels at or slightly above those observed in the baseline may serve to quickly bring the network back into the more optimal oscillatory state as defined by intermediate oscillations amplitudes. This constructive role of ongoing oscillations also provides a biologically plausible explanation for their presence in cortical areas during attentive conditions and their absence during drowsiness.

In the following, I discuss the value of the interpretations of our results within the physical frameworks of self-organized criticality and stochastic resonance.

7.1 Why search for self-organized criticality in the brain?

I have often been asked why it would be interesting to find SOC in the brain. I would therefore like to comment on the relevance of investigating neural dynamics for SOC.

The most obvious benefit of the SOC framework, as it has been used in this Thesis, has been to motivate the hypothesis of long-range temporal correlations of a power-law form, which is not intuitively trivial from a physiological point of view. Technically, the inspiration from statistical physics led to the use of the detrended fluctuation analysis method, which has some advantages over alternative methods for estimating long-range correlations in non-stationary data [103, 104]. For the future research, the demonstrated scaling laws pose novel and unit-independent quantitative constraints on computational models of network oscillations and should thus improve the interaction between experiments and modeling efforts. In fact, as it was argued in Sections 2.3–2.4, evidence for power-law scaling behavior is a promising starting point for attempts to model a system's behavior, since the lack of characteristic scales suggests that all regimes of the observed dynamics rely on the same rules.

The scaling exponents also provide novel indices of neuronal dynamics, which could be useful, e.g., for the study of neurological or psychiatric disorders, or for quantifying the effect of pharmacological substances on the integrity of neuronal activity across many time scales. Finally, by establishing other analogies between SOC systems and the brain one may find additional valuable short cuts to hypotheses about neuronal network structures and

dynamics that are not evident from a physiological perspective. Although these prospects are still speculations, such statistical approaches have proven useful in the analysis of heartbeat dynamics, which has a longer tradition for variability analysis on many time scales [62, 64].

The thorough understanding of the self-organization process that drives complex systems to the critical state and the properties of the spatio-temporal organization and dynamics in the critical state convey a deep insight, at least conceptually, into a lot of complex systems and phenomena in nature (for reviews see [12, 27, 140]). Likewise, the empirical evidence for SOC in neural systems supports our intuition about the brain. Of course there is always a risk that analogies are misleading. Nevertheless, considering the similarity between the physiological properties of neuronal networks and the prerequisites of SOC (cf. Section 3.4.1) it is difficult to see how the SOC framework could not be relevant for our understanding of variability in the brain—from membrane processes to learning, memory, cognition, and behavior, which have all been implicated with scale-free dynamics [18, 31, 54].

Once the above comments are in place, I think that ultimately the importance of SOC to science is its reflection of unity in nature. The prospects that fundamental laws governing the emergence of spatial structures and the propagation of activity in many inanimate complex systems may also play a crucial role for the operation of the brain is fascinating.

Finally, one may also turn the question around and ask whether the science of complexity would benefit from evidence for SOC in the brain? I definitely think the brain provides an interesting "model system" for exploring complexity both empirically and theoretically. The brain has some convenient features from an experimental point of view as it can be modified more easily than many of the other complex systems under study, e.g., biological evolution [11], earthquake [13] or forest-fire dynamics [87]. Last but not least, as argued in the following Section (7.2), there may be a range of interesting functional consequences of self-organized criticality in the brain that have no meaning in inanimate systems.

7.2 Possible functional implications if the brain exhibits SOC

Our data have provided evidence that the ongoing and spontaneous large-scale activity of the brain may be subjected to the same statistical laws as numerous other complex systems in nature (P1 and P5). From a physicist's perspective this may not be very surprising, but from a biological point of view this is interesting because the brain, e.g., unlike the crust of the earth, presumably could have avoided this phenomenon during the evolutionary selection of neuronal properties. In other words, if critical dynamics would have adverse effects on the performance of neuronal networks, it probably would not appear in the brain. It is therefore natural to ask whether SOC dynamics could instead offer a beneficial state or context for neuronal computations.

Indeed there have been proposals that this may be the case, although the empirical evidence mostly relies on analogies with other complex systems operating near a critical point or numerical simulations. Examples of features that may render the SOC state desirable from a functional perspective are:

1) The dynamics in the critical state is highly susceptible to perturbations and may therefore support swift re-organization of neuronal activities when the networks are imposed with processing demands [3, 20, 33] (see also P1, P3, and P5).

2) Scale-free networks tend to be more immune to local failures than random exponential networks [2, 139].

3) Although the critical state is characterized by pronounced variability, it is also an attractor for the dynamics, i.e., the system will always seek back to the critical state if transiently perturbed away from this dynamic point. In this sense, SOC may be viewed as a form of homeostasis. Although homeostatic control has traditionally implied the constancy of a given parameter, recent years of research have revealed a tremendous variability over time of physiological parameters that previously were regarded more or less constant because of

homeostatic control—and the evidence suggests that healthy subjects are characterized by even more variability than patients [63, 64]. It seems that the dynamics in the critical state conveniently separates two pathological regimes, namely, the ordered and regular state with little ability to adapt and the strongly disordered state with random fluctuations.
4) Critical dynamics in the networks may help prevent that the activity gets trapped in the non-optimal regimes of high or low activity, as indicated by the stochastic-resonance relationship between ongoing activity and psychophysical performance (P6). Critical systems only rarely become trapped in a low-dimensional attractor state.

7.3 Outlook and perspectives

Leaving the fascination for conceptual understanding and the quest for general laws of nature aside, scientists also have the obligation to search for and communicate the possibilities of turning fundamental research projects into technologies that benefit society. This Thesis has touched upon two issues where a real breakthrough would make an important contribution to life outside the laboratory.

One issue is related to the complexity of the dynamic state of the brain and its importance for the processing of incoming information from our sensory environment. I believe that the brain's ability to robustly perform computations, transfer, encode, or retrieve information reliably and rapidly within the central nervous system cannot be understood properly without taking the spatio-temporal nature of endogenous activity and the complex topology of the underlying neuronal networks into account. This is why the origin, character, and functional significance of neural complexity deserve attention. The spin-off from elucidating the crucial mechanisms—or rules—by which the brain computes has obvious potentials in terms of developing biologically inspired algorithms to solve complex problems [21]. Understanding the importance of complexity for the functioning of the normal brain should also help us diagnose and develop treatments for neurological and psychiatric disorders.

The other breakthrough that could emerge from the study of neural complexity relates to the potential for discovering novel methods for characterizing, modeling, controlling, or predicting the dynamical evolution of complex systems in general. Humans often strive for stability, e.g., in financial, political, or ecological systems, yet little evidence suggests that changes in such complex systems can actually be controlled or predicted. Profound insight into the nature of complexity has the prospects of improving the reasoning behind and means of making changes in complex systems—whether the insight is gained from the study of models of earthquakes, financial markets, or neuronal networks may not matter much.

People have commented to me that these ideas are philosophy, but I consider it science with perspective.

8 Conclusion

This Thesis has presented evidence that concepts and theories of physics dealing with self-organization and resonance in stochastic nonlinear multi-unit systems are useful for untangling the character and functional significance of complex variability in neural systems.

In particular, it was discovered that ongoing network oscillations at around 10 and 20 Hz in humans exhibit long-range correlations and power-law scaling behavior, which together with the high susceptibility and large variability in amplitude, duration, and recurrence observed for these oscillations, may find a unifying explanation within the theory of self-organized criticality.

Moreover, it was revealed that ongoing neuronal activity can provide a beneficial source of endogenous noise in that the ability to detect consciously and respond behaviorally to weak somatosensory stimuli was optimal at intermediate levels of ongoing sensorimotor oscillations. These findings are consistent with a mechanism of intrinsic stochastic resonance between self-organized critical and exogenous activities, which could be of great importance for central nervous system function in general and account for some of the variability in the way we perceive and react to the outside world.

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